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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
ART UNIT	PAPER NUMBER
1653	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary	Application No. 09/003,574	Applicant(s) Tripp et al.
	Examiner Holly Schnizer	Group Art Unit 1653

☒ Responsive to communication(s) filed on *Jun 20, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 8, 11-13, 16, 17, and 23-26* is/are pending in the applicat

Of the above, claim(s) *23 and 24* is/are withdrawn from consideration

☒ Claim(s) *8, 25, and 26* is/are allowed.

☒ Claim(s) *1, 11-13, 16, and 17* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of the Claims

1. The amendment filed June 20, 2000 has been entered. Claims 18-22 have been canceled. Therefore, Claims 1, 8, 11-13, 16-17, and 23-26 are pending, Claims 23-24 are withdrawn from consideration as being drawn to a non-elected invention, and Claims 1, 8, 11-13, 16-17, and 25-26 will be examined on the merits. The Examiner notes that it appears that Applicant intended to amend Claims 17 and 24 since limitations were bracketed or underlined in these claims. However, the Claims were indicated as being "Reiterated" and therefore **an amendment has not been entered in Claims 17 and 24.**

Rejections Withdrawn

2. The rejection of Claims 16-19 as being indefinite for the recitation of "at least about 9 contiguous amino acid region" in part (b) of Claim 16 has been withdrawn in light of the amendment of Claim 16 deleting part (b). The rejection has been withdrawn in the case of Claims 17-19 since they are dependent from corrected Claim 16.

3. The rejection of Claim 25 as indefinite for the recitation of "homolog thereof" has been withdrawn in light of the amendment to the claim deleting the term "homolog thereof".

4. The rejection of Claims 1, 11-13, 16, and 17 under 35 U.S.C 112, first paragraph for scope of enablement has been withdrawn in lieu of a new rejection as given below.

New Rejections

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 11 is indefinite for the recitation of "wherein said protein comprises at least a portion of at least one amino acid sequence selected from the group consisting of..." (emphasis added) making the claim unclear as to whether "the portion" contains part of one of the sequences of the Markush group or part of several of the sequences listed in the Markush group. The claim contains a Markush group which is commonly used form of alternative expression (see MPEP 2173.05(h)). However, the claim is drawn to "at least one" of the members of the Markush group which indicates that more than one of the members of the Markush group is encompassed. Correction is required.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 11, 12, 13, 16, and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an astacin metalloendopeptidase protein isolated from *D. immitis* wherein the protein is encoded by a nucleic acid molecule that hybridizes to the complement of the claimed nucleic acid sequences and wherein the protein selectively binds to an antibody raised against a protein having an amino acid sequence selected from the group of claimed sequences, does not reasonably provide enablement for any protein having any activity which is encoded by a nucleic acid molecule that hybridizes to the complement of the claimed nucleic acid sequences wherein said protein selectively binds to an antibody raised against a protein having an amino acid sequence selected from the group of claimed sequences . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. to make or use the with which it is most nearly connected, to the invention commensurate in scope with these claims.

10. The claims recite proteins encoded by nucleic acid molecules that hybridize under given stringent conditions to the complement of the nucleic acid molecules having specific sequences

claimed and wherein the protein selectively binds an antibody raised against a protein having one of the amino acid sequences specifically claimed. Therefore, the breadth of the claim includes any protein having any function and derived from any source. Also, the claimed proteins may be any size and can have essentially any sequence. As explained below, the proteins must only be encoded by a nucleic acid molecule with a small stretch of nucleotide sequence having high similarity to the nucleic acid sequence of the present invention and they may have an epitope in common with the proteins of the present invention. With respect to the hybridization conditions, the claim limitation that the protein must be encoded by a DNA molecule that hybridizes under given stringent conditions to the DNA molecules having SEQ ID NOs: 1, 2, 29, 30, 32, or 33 encompasses proteins varying widely in structure and function. Such hybridization conditions permit the hybridization of nucleic acid molecules having a low overall sequence identity and the claim would include proteins encoded by nucleic acid molecules completely unrelated to those disclosed. For example, a nucleic acid molecule having less than 40% overall identity to the nucleic acid molecule of SEQ ID NO: 1 in claim 1 may hybridize to the nucleic acid molecule of SEQ ID NO:1 solely because a small region of the nucleic acid molecule has 100% identity to that of SEQ ID NO:1. Such a protein may not have any structural or functional similarities to the proteins having the sequences disclosed in the specification. Thus, the hybridization conditions only limit the claims to a protein encoded by nucleic acid molecules of any size and essentially any sequence. The claim limitation that the protein binds selectively with an antibody raised against the proteins having the disclosed and claimed sequences again encompasses proteins

having a wide variety of functions and structures. At most, the claim is limited to proteins having small regions (the size of an epitope) of homology. However, antibodies are known to cross-react non-specifically with proteins depending on the conditions of the binding assay and the specification and claim do not provide what binding conditions would prevent such non-specific binding. Thus, the claims are so broad as to encompass proteins having any size, sequence, and function. The specification only discloses deduced polypeptide sequences (SEQ ID NOs: 3-10, 31, and 34) encoded by nucleic acid molecules (SEQ ID NOs: 1-2, 29-30, and 32-33) isolated from *D. immitis*. According to an analysis of the homology of the disclosed sequences to those of the database, it appears that some of the disclosed polypeptide sequences might have astacin metalloendopeptidase proteins while others (SEQ ID NOs: 3, 5, 6, and 8-10), missing a sequence motif known to be essential for astacin metalloendopeptidase function, do not.

11. The only working examples given in the specification are limited to the deduced amino acid sequences of SEQ ID NOs: 3-10, 31, and 34, the specification does not provide any examples of an antibody which will bind the disclosed protein, and there is no suggestion as to the identity of the epitopes in any of these sequences or as to whether these epitopes are unique to *D. immitis* or even to parasites. Such information is essential to the utility of the protein as an agent in the diagnosis of parasitic infections because antibodies made to proteins containing epitopes that are not species specific will cross react with proteins from other species giving false positive results making the diagnosis of parasitic infection impossible. Moreover, antibodies are known to cross-react non-specifically with proteins depending on the conditions of the binding assay, and

the specification and claim do not provide what binding conditions would prevent such non-specific binding. Therefore, in view of the empirical nature of the antibody binding, the unpredictable nature of the art and lack of guidance with respect to the appropriate modifications, one skilled in the art would have to make and test all nucleic acids that meet the hybridization limitations, make a large number of antibodies to the specific proteins disclosed in the specification in hopes of finding one that is specific for D. immitis or even just parasites, and then test the proteins encoded by the innumerable nucleic acid molecules to determine if they bind any one of the antibodies. This amount of experimentation is extremely extensive. In the case that the proteins would actually be used for their activity, the skilled artisan would need to determine the function of the protein so that the protein could be used. Therefore, based on the empirical and unpredictable nature of the invention, the limited guidance, the lack of working examples, it would require an undue experimentation to identify the proteins encompassed by the claims and if or when such a protein was identified it would require undue experimentation to determine how to use the protein encompassed by the claims.

12. The same discussion as given above also pertains to portions of the protein (claim 11). As explained above, the specification has not taught what portions of the proteins would be functional (either in astacin metalloendopeptidase activity or as a diagnostic agent). Addition of the limitation that the claimed proteins contain an "extended zinc-binding domain motif" (Claim 12) also does not enable one of skill in the art to use the invention because the specification does not teach what other regions of the protein are necessary for its utility or what modifications can

be made to the protein and still maintain its function. Compositions comprising the claimed protein (Claims 16 and 17) and the protein of claim 1 produced recombinantly (Claim 13) also lack enablement for the reasons set forth above.

13. The examiner notes that this rejection would be overcome by removal of SEQ ID NOs: 3, 5, 6, 8, 9, and 10(since these sequences do not appear to be metalloendopeptidase proteins and appear to have sequences unrelated to the other claimed sequences) from the claim and amendment to the claims adding the limitation that the claimed proteins have astacin metalloendopeptidase function and are isolated from *D. immitis*.

14. Claims 1, 11, 12, 13, 16, and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15. Applicant is referred to the interim guidelines on written description published December 21, 1999 in the Federal Register, Volume 64, Number 244, pp. 71427-71440 (also available at www.uspto.gov) and the Training Materials also available at www.uspto.gov.

16. The written description requirement for a claimed genus may be achieved by sufficient description of a representative number of species by relevant identifying characteristics (Eli Lilly, 43 USPQ2d 1398, 1406 (CAFC 1997)). The "representative number" is inversely related to the predictability of the art. In the present case, the genus is any protein which: 1) is encoded by a

DNA molecule that hybridizes under given stringent conditions to DNA molecules having specifically claimed sequences and, 2) selectively binds to an antibody raised against a protein having specifically claimed amino acid sequences. Whereas, the specification only discloses deduced polypeptide sequences (SEQ ID NOs: 3-10, 31, and 34) encoded by nucleic acid molecules (SEQ ID NOs: 1-2, 29-30, and 32-33) isolated from *D. immitis*. Some of the disclosed polypeptide sequences appear to be astacin metalloendopeptidase proteins while others (SEQ ID NOs: 3, 5, 6, and 8-10) do not since they appear to lack a zinc binding domain essential for astacin metalloendopeptidase function.

17. In evaluating evidence of possession, factual considerations are weighed in view of the level of skill and knowledge in the art. The factual considerations include a description of a complete structure, physical and/or chemical properties, functional characteristics, correlation between structure and function, method of making, and combinations of the above. In the present case, the scope of the claims includes a vast number of proteins, having any size, various structures, and any or no activity. The specification and claim do not indicate what distinguishing attributes are shared by members of the genus. The only characteristics given in the claimed genus is that the protein is encoded by a nucleic acid molecule that hybridizes to the disclosed nucleic acid molecule sequences and that the protein cross reacts with an antibody that binds the disclosed proteins. As discussed below, these limitations are extremely broad. With respect to the hybridization conditions, the claim limitation that the protein must be encoded by a DNA molecule that hybridizes under given stringent conditions to the DNA molecules having SEQ ID

NOs: 1, 2, 29, 30, 32, or 33 encompasses proteins varying widely in structure and function. Applicants contend "that such hybridization conditions will permit hybridization between nucleic acid molecules which share about 71% or greater sequence identity" (see p. 9, lines 11-12 of Amendment filed Dec. 21, 1999 (Paper No. 10)). However, such hybridization conditions also permit the hybridization of nucleic acid molecules having a much lower sequence identity and the claim would include proteins encoded by nucleic acid molecules completely unrelated to those disclosed. For example, a nucleic acid molecule having less than 40% overall identity to the nucleic acid molecule of SEQ ID NO: 1 in claim 1 may hybridize to the nucleic acid molecule of SEQ ID NO:1 solely because a small region of the nucleic acid molecule has 100% identity to that of SEQ ID NO:1. Such a protein may not have any structural or functional similarities to the proteins having the sequences disclosed in the specification. Thus, the hybridization conditions do not limit the claims to a protein encoded by a nucleic acid molecule with 71% homology to the claimed specific sequences. In contrast, without a limitation on the activity of the encoded protein, the claims are drawn to proteins having any function, structure, chemical, and/or physical characteristics. The additional limitation that the protein must cross react with an antibody that is raised against the disclosed proteins does not do much to narrow the size of the genus. The specification does not show or describe an essential element in the claim; an antibody that binds the proteins having SEQ ID NOs: 3, 4, 5, 6, 7, 8, 9, 10, 11, 31, or 34. Thus, in addition to failing to describe any structural characteristics of the claimed protein, the specification also does not describe any structural characteristics of an antibody which is essential to obtaining the claimed

proteins. The specification only provides a deduced amino acid sequence of the proteins which are disclosed therein and does not provide any structural information such as the regions or sequences of the protein which contain the epitopes. Likewise, the specification does not provide epitopes that are specific to the proteins of SEQ ID NOs: 3, 4, 5, 6, 7, 8, 9, 10, 11, 31, or 34 or even specific to parasitic proteins. Thus, while the claims may be limited to proteins which contain an epitope in common with one of the sequences disclosed in the claim, the specification is silent as to what the epitope would look like. As such, the specification fails to describe a representative number of species by relevant identifying characteristics.

18. In addition, the claim provides no functional limitation to the proteins and thus encompasses proteins having a wide variety of functions or no function at all. The specification describes astacin metalloendopeptidases. Some of the sequences provided appear to have homology with metalloendopeptidase proteins. However, it appears that some of the protein sequences claimed (e.g. SEQ ID NOs: 3, 5, 6, and 8-10) lack a zinc-binding region essential for metalloendopeptidase activity. Therefore, it appears that it is unknown as to the function of these proteins. Thus, the functional characteristics of the claimed proteins have not been sufficiently described in the specification.

19. In summary, as explained above, the scope of the claim includes numerous structural variants. The genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the

genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because a specific, not general guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is extremely variant, the disclosed SEQ ID NO:s alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the claimed genus.

20. The examiner notes that removal of SEQ ID NOs: 3, 5, 6, 8, 9, and 10 (since these sequences do not appear to be metalloendopeptidase proteins) from the claim and limiting the claimed protein to an astacin metalloendopeptidase protein would overcome this rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached Monday-Friday from 7:30 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 306-4119. The fax phone number for Official Papers to this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen Cochrane Carlson PhD

Holly Schnizer, Ph.D.
August 31, 2000

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER